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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/075,947	02/13/2002	Nai-Kong V. Cheung	MSK.P-013-2	9846

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EXAMINER	
HELMS, LARRY RONALD	
ART UNIT	**PAPER NUMBER**
1642	

DATE MAILED: 10/04/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/075,947	CHEUNG ET AL.	
	Examiner	Art Unit	
	Larry R. Helms	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 July 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *11,23 and 29-41* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *11 and 38-41* is/are rejected.

7)☒ Claim(s) *23 and 29-37* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *6/5/02*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's election of Group III, claim 11 in the reply filed on 7/12/04 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). In addition because all of the amended and newly added claims are directed to T cells, the restriction is moot.

Claims 11, 23 have been amended, claims 1-10, 12-22, 24-28 have been canceled, and claims 29-41 have been added.

Claims 11, 23, 29-41 are pending and under examination.

2. NOTE: The examiner acknowledges that the amendments to the specification filed 6/5/02 has been entered.

Specification

3. The disclosure is objected to because of the following informalities:

A. The first line of the specification needs to be updated to indicate application 09/142,974 is now US Patent 6,451,995.

B. The title of the invention is not descriptive of the invention to T cells. A new title is required that is clearly indicative of the invention to which the claims are directed.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claim 41 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 41 recites the limitation "therapeutic moiety" in claim 39. There is insufficient antecedent basis for this limitation in the claim.

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

7. Claims 11, 38-41 are rejected under 35 U.S.C. 103(a) as being unpatentable over Eshhar et al (US Patent 5,912,172, with priority to at least 4/90) and further in view of Bernhard et al (Int. J. Cancer 55:465-470, 1993) and Hansen (US Patent 5,851,527, with priority to 4/88) and Epenetos et al (US Patent 5,973,116, priority to 1/93).

The claims are drawn to T cells that express a single chain antibody encoded by a polypeptide wherein the single chain antibody is a anti-GD2 antibody and wherein the polynucleotide encodes an additional therapeutic toxin or a pro-drug converting enzyme or streptavidin.

Eshhar et al teach T cells that express a single chain antibody encoded by a polypeptide wherein the antibody has specificity for a tumor antigen (see entire document). Eshhar et al teach cloning of the VH and VL from a hybridoma (see Figure 10 and column 5, lines 49-66). Eshhar et al does not teach the GD2 antigen or an

additional toxin, pro-drug converting enzyme or streptavidin. These deficiencies are made up in the teachings of Bernhard et al, Hansen, and Epenetos et al.

Bernhard et al teach a bispecific anti-GD2Xanti-CD3 antibody to target tumor cells and lysis by targeting T cells to the tumors by binding of CD3 on the T tells and GD2 on the tumor cells.

Hansen teach antibody enzyme conjugates, wherein the enzyme is a pro-drug converting enzyme (see column 2, lines 45-60). Hansen also teach the radiolabeling with Tc-99m (see column 6, line 45) and a method for detecting the presence of the antigen in tissue (see column 19, lines 15-25).

Epenetos et al teach the production of single chain antibody molecules with an additional protein of streptavidin, polynucleotides encoding such and polypeptides as well as labeling of the proteins (see example 4, and column 16, lines 37-42).

It would have been prima facie obvious to one of ordinary skill in the art at the time the claimed invention was made to have produced a T cell that expressed the anti-GD2 antibody and further comprised a toxin, pro-drug converting enzyme, or streptavidin in view of Eshhar, Bernhard, Hansen, and Epentos.

One of ordinary skill in the art would have been motivated to and had a reasonable expectation of success to have produced a T cell that expressed the anti-GD2 antibody and further comprised a toxin, pro-drug converting enzyme, or streptavidin in view of Eshhar, Bernhard, Hansen, and Epentos because Eshhar et al teach targeting tumor cells with a T cell that expresses an antibody and in view of Bernhard et al it would have been obvious to use the anti-GD2 antibody because

Bernhardt targets T cells and tumor cells and the construct of Eshhar targets tumor cells by bringing the T cell to the tumor cell wherein the T cell expresses an antigen on the tumor cell and as taught by Bernhard the GD2 is on tumor cells. In addition, one of ordinary skill in the art would have been motivated to and had a reasonable expectation of success to have produced a T cell that expressed the anti-GD2 antibody and further comprised a toxin, pro-drug converting enzyme, or streptavidin in view of Eshhar, Bernhard, Hansen, and Epentos because Hansen et al teach that enzyme conjugates can effectively target the cells and the agent can then be transformed to a product (see column 5, line 28-36, column 6, lines 61-67, line 57) and the conjugate can also be a toxin. In addition, one of ordinary skill in the art would have been motivated to and had a reasonable expectation of success to have produced a T cell that expressed the anti-GD2 antibody and further comprised a toxin, pro-drug converting enzyme, or streptavidin in view of Eshhar, Bernhard, Hansen, and Epentos because Epenetos et al teach "the cytotoxic portion of the compound of the invention is capable of oligomerization." (See column 10, lines 46-49). Epenetos et al continues "the cytotoxic portion is streptavidin." (See column 11, lines 7-8) and Epenetos et al teach construction of ScFv-streptavidin fusion results in "binding multivalently" as compared to the ScFv without the streptavidin fusion (see column 26, lines 23-38). Thus, it would have been obvious to obtain the amino acid sequence of the anti-GD2 antibody of Bernhard et al from the hybridoma, which obviously Bernhard was in position because they produced the monoclonal antibody, and express the single-chain antibody of Bernhard et al in a T cell as described by Eshhar to target tumor cells and add a toxin or

drug converting enzyme or steptavidin because Hansen or Epenetos et al teach conjugation of these molecules for diagnosis, treatment, or increased avidity.

Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references.

Conclusions

8. Claims 23, 29-37 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Larry R. Helms, Ph.D, whose telephone number is (571) 272-0832. The examiner can normally be reached on Monday through Friday from 6:30 am to 4:00 pm, with alternate Fridays off. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffery Siew, can be reached at (571) 272-0787.

10. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center. The faxing of such papers must conform with the notice published in the Official Gazette,

1096 OG 30 (November 15, 1989). The Fax Center telephone number is 703-872-9306.

Larry R. Helms

571-272-0832